

# THE MÜTTER LECTURES ON SELECTED TOPICS IN SURGICAL PATHOLOGY.

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LECTURE VI.

## TETANY—TETANUS.

**SYLLABUS.** *Tetany*.—Definition and theories of its causation. Frequency after thyroidectomy. In the past has often been mistaken for tetanus. Semeiology and symptomatology. Researches concerning the thyroid body. Experiments with its extirpation and transplantation. Relationship of tetany to myxœdema and cachexia strumipriva. Acute mucin poisoning. Deductions as to the safety of certain operations on the thyroid.

*Tetanus*.—Consideration of the wounds, the wounded and their environment, when dealing with the subject. Class of wounds most often infected. Predisposing causes and circumstances of age, sex, color, climate and mental condition. Influence of weather and other conditions of locality. Tetanus hydrophobicus and tetanus neonatorum essentially the same as the traumatic form.

Theories as to its causation. Theory of its nervous origin. The humeral theory and that of its zymotic origin. Discovery of its specific microbe by Nicolaier, and confirmation and elaboration of his work by Kitasato. Description of the bacillus of tetanus. Discussion of its peculiarities and specific action after inoculation. Deductions as to possible treatment of the disease.

**T**HOUGH tetanus and tetany are not merely similar in name, but present many characteristics which might lead to mistaking one for the other, there is, nevertheless, such a wide etiological difference between them that a clear differentiation is of the greatest importance, not merely for the

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sake of accuracy, but for the credit of surgery and the welfare of an important class of patients, *i. e.*, those suffering from enlargements of the thyroid.

Both occur as sequels of operative interference, and if tetany is so infrequent as never to be seen by some, it may be experimentally produced and studied almost at will.

Tetany may be described as apparently a neurosis, manifested especially by tonic spasms, particularly of the extremities, and an increase of mechanical and electrical excitability of peripheral nerves. It is pathognomonic of the disease that these spasms may be produced by compression of one of the great arterial or venous trunks.

It was described first by Corvisart and Trousseau, and then more fully by Erb and Chvostek. It occurs spontaneously in less severe form in pregnant and nursing women, in children after exposure to cold, or after such intestinal lesions as may be produced by typhoid or by parasites; also among young apprentices to certain trades. It occurs also in endemic or epidemic form. But what interests us most here is that it sometimes follows certain operations, and extirpation of the thyroid in particular, and then constitutes so serious a complication that a large percentage of patients succumb.

It has been described under various names besides tetany, as, *e. g.*, tetanella, idiopathic muscular spasm, carpo-pedal cramps or spasms, etc. It is certainly a functional neurosis, comprising spasms of muscles in a pretty regular order or rhythm. Patients do not lose consciousness.

It was considered by Herz to be due to spinal anæmia, while Jacobi, on the contrary, attributes it to meningeal hyperæmia, and Gowers explains it on the hypothesis of a primary lesion in the primary cells of the cerebro-spinal tract. While it is certain that its pathology and symptomatology are still obscure, it will be shortly seen that a notable advance in its experimental study has been recently made.

According to Weiss (*Ueber Tetanie*, "Volkmann's Samml. klin. Vort.," No. 189), it was noted as a post-operative phenomenon in Billroth's clinic. Later it was noted and remarked upon by Schönborn, Albert, Nicoladoni, Mikulicz, Gussenbauer, Corley, Szuman, Kocher, Kothman, Higuget and oth-

ers, and has recently been made the subject of a careful experimental study and an elaborate essay by von Eiselsberg (*Ueber Tetanie in Anschlüsse an Kropfextirpation*, Vienna, 1890), to which I am greatly indebted, and from which I have largely drawn.

The most striking characteristic about tetany is the peculiar severity or malignity which it exhibits when occurring as a sequel to thyroidectomy. Thus Eiselsberg refers to twelve such cases in Billroth's clinic out of fifty-three total extirpations, of which eight died, while in two the disease assumed a chronic character, and only two finally recovered. To its severity and its fatality is largely due the unfortunate confusion of terms and clinical pictures, by which so many deaths after total extirpation of the thyroid have been described as due to tetanus. It is of importance, then, to differentiate accurately between the two diseases.

The symptoms of post-operative tetany may supervene almost immediately after the effects of the anæsthetic have disappeared, or may be delayed so long as ten days. Usually prodromal symptoms give warning of what is coming; such as malaise and a combination of muscular weakness, with a sensation of muscular stiffness. Sometimes these sensations are quite absent and the outset of the disease is equally violent and surprising. Two signs which may be usually early elicited are so characteristic, so diagnostic, that they deserve great emphasis.

The first is Chvostek's. A slight tap upon the side of the face, over the point where the facial nerve emerges from the parotid, suffices to call forth a sudden spasm of that side of the face. The second—Trousseau's—is the spasm of an extremity, which may be produced by compression of its principal blood or nerve supply for a brief period of time, from a few seconds to a few minutes. The first sign is easier of production, is elicited without detriment to the patient, and is pathognomonic; while the second is of no greater value, and may be followed by pain, and its frequent repetition certainly does serious harm to the patient.

The muscles of the face are those commonly first affected; then those of the upper extremity; they are always more

marked in the arms than the legs, and sometimes the latter seem to escape. The position of the hands and fingers is usually that seen in cases of irritation in the course of the ulnar nerve; the elbow somewhat flexed, the hands flexed to the ulnar side, the fingers bent at the metacarpo-phalangeal joints, thence straight and stiff, the thumbs bent into the palms. This position of the hand and fingers is not invariable nor pathognomonic, but is that usually seen. Sometimes the fist is doubled up with the thumb between the first and second fingers. The muscles of the forearm are hard, and sometimes a little tremor may be perceived. It is always difficult to overcome the muscular spasm. In severe cases the hands are usually held with their backs pressed together. When the lower limbs are affected the legs are usually stiffly extended, with strong plantar flexion of foot and toes. With all this muscular spasm there is more or less pain in the affected parts, with temperature usually considerably elevated. Such attacks may last from two to fifteen minutes or more, but they do not occur with nearly such frequency as the convulsive seizures of true tetanus, and it will be seen that there are other wide differences in the onset and march of the two diseases.

Nevertheless, in the most severe form of tetany there may be such contortion of the facial muscles as to resemble the "sardonic grin," and which would, of course, destroy the significance of Chvostek's sign. Tonic cramp of the abdominal muscles is not unknown, especially of the recti, and one may even see a certain degree of opisthotonos.

Dyspnœa may be caused by spasm of the diaphragm or thoracic rigidity, and cyanosis may be the result of cervical spasm. In some cases the patients give shrill cries; others speak with great difficulty. Deglutition is sometimes difficult. Finally in the gravest cases consciousness is lost; and usually at such times spasm relaxes. Death never occurs in the height of the disease, usually hours or days later.

Autopsy gives only negative findings; only twice Weiss found some slight disturbance in the gray matter of the anterior horns in the medulla.

Some peculiar features have been noticed in individual cases. Thus in one of Billroth's cases the patient was four

months pregnant at the time of the thyroidectomy. Normal delivery at term was in no wise interfered with, although for *nine years* she suffered from tetanic seizures, during which Chvostek's and Trousseau's signs could also be easily evoked. For the latter a very brief compression of the ulnar nerve sufficed. Overwork or excitement, particularly in cold weather, seemed to precipitate these attacks. Her temper appeared less equable than before the operation, and she was at times found almost uncontrollable. Before the operation, too, she had suffered spontaneous loss of hair and nails; these were afterward as spontaneously restored.

Another and younger woman recovered, but long remained subject to mild attacks, which occurred much oftener in cold than in warm weather. After a couple of years she had no seizures properly speaking, but the phenomena described by Chvostek and Trousseau could be elicited at almost any time.

Weiss has described (*Allg. Wiener Med. Zeit.* 1885, No. 37.) an atrophy of those groups of muscles most involved in the spasms, as a sequel of tetany, though not of that observed after thyroid extirpation. So also falling of the hair has been noted by Kocher (*Arch. f. klin. Chir.* 1883) as an accompaniment of cachexia strumipriva, and by English writers among the symptoms of myxœdema.

In one of the marked fatal cases, and in two of the others, a great temporary improvement was noted after a profuse sweating. Whether this might be of service as a hint in the therapeusis of the affection is a question worth considering.

It will be noticed that all of Billroth's twelve cases were females. Of the eight fatal cases, as detailed by Eiselsberg, I have tabulated the following information: (See table, p. 130).

Though so rare among males the disease is not unknown among them, since Mikulicz has reported two cases and Higguet one.

No treatment seemed to be of avail, and nothing seemed to mitigate the intensity of an attack. The internal use of chloral with the subcutaneous exhibition of morphia seemed most satisfactory. In view of a remark made above, I would suggest the expediency of trying pilocarpine as a diaphoretic.

When these and similar cases are critically studied it appears

that their ætiology is inseparably connected with the total removal of the thyroid. They were in no wise nor remotely septic. In the eight fatal cases above alluded to only once was there the slightest suppuration in or about the wound. So with the cases reported by others; wound disturbance of any kind was the rare exception. To be sure in the very few cases reported where pus has collected in the wound the violence of the symptoms increased, but pressure upon the scar at almost any time would have the same effect; and in other cases it was noticed that a constrained position in bed affected one patient in the same way, and in another, apparently about recovered, a warm bath precipitated a violent attack.

<i>Age.</i>	<i>Attack Began, Days After Operation.</i>	<i>Lived How Long, After First Attack.</i>
12	Fifth.	Three months.
18	First.	Three days.
39	Tenth.	One day.
64	Ninth.	Eight days.
17	Second.	Seven months.
23	First.	Three days.
36	Fourth.	Four days.
32	First	One month.

Injury to the recurrent laryngeal nerve does not explain these cases, since this nerve is practically always injured in these operations. We are confronted with the following most significant figures: After 53 total extirpations it occurred 12 times; after 11 partial extirpations it did not occur at all. It has occurred twice, once to Szuman, once to Billroth, to see mild cases of tetany after nearly complete removal of the thyroid body. The inference, then, is unavoidable that in some way, not yet understood, the removal of the thyroid

brings about the curious phenomena collectively termed tetany. *How or why* this is the case is a problem to be solved—if at all—only by experiment. This is made the more difficult by lack of exact knowledge of its function.

The names of A. Bardeleben, Schiff, Zesas, Colzi, Wagner, Albertoni and Tizzoni, Sanguirico and Canalis, Fuhr, Munk, Horsley, Carle and others less well known, have heretofore figured prominently in researches upon this organ. As the result of their labors it has been pretty well settled that in cats and dogs removal of the healthy thyroid provokes a constant diseased condition which is fatal; while sheep, rabbits and rats tolerate it without harm. Further, when it is made *a deux temps* the symptoms only appear after removal of the second half. Extirpation of a lateral half only is seldom provocative of disturbance, while Wagner, Horsley and Rogovitsch have seen a compensatory hypertrophy of the remaining portion. (Vid. Sutton's *Dermoids*, p. 83-4.)

Schiff went further and experimented with transplantation. It is now known that this peculiar organ, or ductless gland as it is often called, possesses the peculiar property of usually first quickly contracting adhesions in any new tissue in which it may be placed, and then later of establishing for itself an adequate vascular supply with, presumably, more or less restoration of its function.

Schiff claimed that when an animal, into whose peritoneal cavity the thyroid of another of its own species had been transplanted, subsequently had its own thyroid totally removed it did not develop these peculiar symptoms. But these results claimed by Schiff have been positively denied by others, and certainly need confirmation. At all events it seems pretty clear that dogs and cats very seldom survive removal of the entire thyroid, and that in those who do accessory thyroid bodies are found. It was Fuhr who especially determined this matter, to disprove the claims of Kaufman and Tauber; and he further showed that no amount of irritation of the recurrent nerve sufficed to provoke tetany—only total thyroidec-tomy would produce it. Horsley has shown that virtually the same obtains in the case of monkeys, who develop tetanic

symptoms and fall into a condition of myxœdema, in which mucin is found in considerable quantities in certain tissues and in the blood.

In order to better determine the influence of the thyroid relative to these peculiar nervous phenomena Eiselsberg made experiments on a series of 100 cats, having selected this animal because it seems to be free from accessory thyroids whose presence, by subsequent compensatory hypertrophy, might vitiate the results.

In one series he made total extirpation 17 times. Only once did suppuration occur, the other 16 wounds healing *per primam*. All these animals developed tetany; the youngest displaying its characteristic signs almost immediately after awakening from the narcosis, the others in from one to three days. All died of the disease. The symptoms in animals consist of tremors and muscular spasms which show themselves particularly as the creatures rise from the recumbent position or still more from the dorsal. Dyspnœa is frequent. Then tonic spasm of the extremities supervenes, and this can be produced almost at will by tapping the limb over the greater nerve supply. During pauses they are usually quiet and apathetic. They usually die in spasm. The course of the disease is usually about a week, but it may be fulminating and kill them in a day. Loss of appetite and rapid emaciation are conspicuous. The act of deglutition frequently provokes an attack. Free flow of saliva is often noted; during this there is sometimes temporary improvement. The limbs often assume rigid positions, reminding one of catalepsy.

Nine times total extirpation with transplantation was tried—once under the skin of the neck, twice under that of the belly, twice between muscles, twice in the peritoneum, and twice as Schiff did it. Seven times out of nine these wounds healed *per primam*. All nine died of tetany.

In 1887 Ewald reported (*Ber. klin. Wochschr.*, 1887, No. 11) that after hypodermic injections of thyroid juice into healthy animals, some disturbance—lasting 1—2 hours—was produced. But according to Horsley this has no different effect from other tissue juices which contain some fibrinogenous poison. With this in mind Eiselsberg made five total extirpations, after

which a strong extract of the thyroid was injected under the skin, without any apparent effect. In two other animals he substituted a small dose of morphia, by which both animals were made more quiet, but all seven died of tetany. He then tried a fourth series of sixteen, extirpating only a lateral half. Two animals died of infectious pneumonia, the other fourteen all recovered, without any appearance of tetany. In eleven others the extirpated half was transplanted into the peritoneum, with the same negative result.

Twice he followed Schiff's experiments, and extirpated first one half and then the other, transplanting the second half into the peritoneum, and both animals died of tetany. Nine times this experiment was so varied that *the first half* removed was transferred, while the other half was extirpated from 3 to 21 days later. Eight of these animals showed perfect wound healing, but died of tetany; only one of these, an old and large animal, with a period of 3 weeks intervening between the two operations, recovered without disturbance.

These results correspond exactly with Carle's obtained on dogs. In four of this last series of nine cases it is noteworthy that between the first and second operations a considerable hypertrophy of the undisturbed half had taken place, and when this second and enlarged half was taken away, in each instance the tetany was of the fulminating variety. Only once out of four other cases in which the first half was transplanted between the peritoneum and its overlying fascia, did perfect fixation and organization—*i. e.*: vicarious restoration of function (?)—take place; the other three died of tetany.

Seven other experiments, by which more than half of the total thyroid mass was removed, seem to demonstrate that when four-fifths of this body is taken away, tetany is the almost inevitable result. In sixteen other animals vascular exclusion of the thyroid was made by ligation of all its vessels. All of these developed tetany, and all but four died of it; the four gradually recovered. When the two halves were thus excluded at intervals of six weeks, there was no apparent effect.

These numerous experiments certainly seem convincing though the obvious inference is not in accord with the views of Munk and Drobniak, who are disposed to regard the tetany

as due to irritation in and about the wound upon the large nerves closely adjoining, and who ascribe to suppuration the *role* of being the irritant factor. It will be seen that 87% of wounds in those animals which Eiselberg operated upon healed without suppuration, and that this union *per primam* did not seem to interfere with the onset of tetany. Moreover, Horsley, Fano, Ewald and Weil have abundantly shown weaknesses in Munk's chain of argument, and have apparently disproved his contradictory statements, showing the fallacies of his reasoning and the inaccuracy of his methods.

Although it takes us away from our primary subject, which is rather a discussion of the ætiology of two diseases presenting certain points of resemblance yet widely different in pathogeny, still we may with profit consider for a moment what relation tetany, following thyroidectomy, bears to myxœdema and to cachexia strumipriva, following the same procedure. The two latter are eminently chronic maladies, while the former is essentially acute. We are largely indebted in this consideration to the Myxœdema Committee of the London Clinical Society (Appendix to their Trans., 1883), and especially to Horsley's experiments upon apes. This investigator saw sometimes a rapidly fatal tetany, which has been spoken of as acute experimental myxœdema, while in other cases there developed slowly the well known signs of the common form, depending very largely upon the temperature at which the animals were kept, since the colder the environment the more quickly they died, and with more acute symptoms. In the first stage of myxœdema there is a marked increase of mucin secreted by the salivary glands, intestines and bladder, while on autopsy it is found in the blood and in abnormal quantities in certain tissues. The influence of temperature is beautifully demonstrated in an instance reported by Horsley. A sheep underwent total extirpation, and remained apparently well for twenty months; he was then, after shearing, exposed to cold, after which he developed acute symptoms and died a typical death. From all of which it appears that tetany and myxœdema are, as it were, interchangeable diseases; dependent on the same causes, differing only in march and course. It follows from this that the thyroid is an organ not only of pecul-

iar function, but that it is one of the most indispensable parts of our bodies. Of several hypotheses which have been advanced to account for its peculiar importance, that which seems best to explain the facts, and, indeed, perhaps the only one tenable, is that it has to do in some way with the transformation of mucinous substances which when allowed to collect in the system certainly are injurious and even fatal. As corroborating this view, we know a peculiar bronchial catarrh which these patients occasionally present, with its tenacious mucinous secretion; further that with the subsidence of this elimination the disease is commonly augmented.

Furthermore, that with profuse salivary or sudoriparous excretion amelioration occurs, and that when excretion is hindered, as by cold, the symptoms are at once changed for the worse. It appears that by such symptomatic discharges the flooding of the organism with mucin is prevented. Finally, the very common colloid, or, more exactly, mucoid degeneration of the thyroid body has a significance which must not be overlooked; as if, according to Eiselberg, when this organ can no longer bring about the proper conversion of mucin (or its allied substances) it collects it in reservoirs in the shape of colloid material, which is, at least, difficult of resorption, and so keeps it out of the economy.

These views gain credence also from the undeniable fact that excess of mucin is poisonous to the system, and this has been beautifully demonstrated by Wagner. He injected mucin which had been carefully extracted from the salivary glands of cattle, into cats, and produced thereby typical tetany.

The occurrence of idiopathic tetany appears to have much to do with meagerness of diet or improper nutrition. Neusser has called attention to a certain similarity between pellagra, as he studied it in Austria and Roumania, and epidemic tetany among school children. Each appears to be in no small measure an auto-intoxication brought about by unwholesome food. Most interesting and important in this connection is Gerhardt's discovery that tetany sometimes follows dilatation of the stomach, with its train of fermentative mal-digestive disturbances.

Obviously, certain difficulties present themselves in accept-

ing these views. Why should certain animals display so violent manifestations after thyroidectomy, while other species or genera are scarcely or not at all affected? Why should the carnivora belong to the former class, and the herbivora to the latter, as to a large extent they do?

Beyond stating that the herbivora appear to be exempt from the acuter manifestations, we can give no answer to such questions unless it be found in the nature of their diet. It is of interest here that at least one patient who made a good recovery after thyroidectomy noticed a notable change in his own appetite, since he reported to Eiselsberg that he had lost all wish for meat and had become a vegetarian (loc. cit. p. 35, note).

Another query naturally arises here. Why do some persons to all appearances completely recover after thyroidectomy, while others succumb quickly to acute tetanic manifestations, and yet others fall into the most sad condition of myxœdema? As yet this can only be partially answered. Yet it is known that in youth the thyroid plays a more important part than in latter adult life. It is also quite sure that when we attack the thyroid it is because it is no longer in a physiological but a pathological condition, and when we draw inferences between clinical experiences and experimental results we must bear this in mind. Moreover, it appears safer, so far as the disease at present considered is concerned, to remove a cancerous thyroid than a goitre. Moreover accessory or supernumerary thyroids are frequently found, often at points where they are difficult of recognition, as behind the larynx, at the root of the tongue, etc., and when present they can of course assume an importance begotten of necessity. To this I might add the possible assumption of function, in certain cases, by such correlated tissues as the tonsils or other lymphoid tissues, or possibly even the bone marrow, although nothing definite is yet known upon the matter.

Although it bears little if at all on the pathology of tetany I deem it quite advisable here to introduce a very brief notice concerning some recent and very important studies concerning the curability of myxœdema, taken in the main from a recent note in the *Therapeutic Gazette*, (Oct. 1890, p. 718).

Early in 1890, Mr. Horsley suggested that the disease might

be cured by transplanting healthy thyroid tissue into the bodies of patients thus suffering. But it appears he was forestalled in the idea by Bircher, who related certain valuable results obtained by this method. He described an acute case in a female patient from whom, unintentionally, the whole gland had been removed. Severe symptoms supervening, Bircher in January, 1889, transplanted into the abdominal cavity a portion of an apparently normal tissue from a goitre. The immediate effect was very happy and the patient returned to work. Three months later, however, it became evident that the transplanted portion had atrophied, as myxœdema again appeared and progressed. A second transplantation was then made with more lasting improvement, as the patient remained fairly well for nine months. At time of writing the symptoms had returned in very mild degree, but the beneficial effect was established indubitably.

In the *Brit. Med. Jour.* for July 26, 1890, Horsley reports that he had recently learned from Kocher, of Berne, that he attempted to obtain the same effect in 1883, by the same method, but that the graft was too soon absorbed. Further, that after hearing of Bircher's success, Kocher took up the subject again, in 1889, by transplanting, in two cases, half of a thyroid body into the abdomen, fixing it to the wall by sutures. In each case the gland was, after a time, "aseptically exfoliated." Then in three cases he put the gland loose in the abdominal cavity. The final results of these cases have not yet appeared, though at least one was greatly improved.

From these considerations Mr. Horsley thinks that the operation should be performed not only in cachexia-strumipriva, but also in myxœdema and sporadic cretinism. But whether the transplanted gland-tissue may better come from a human being or from an animal remains to be decided.

There is perhaps no *terra incognita* in physiology in which ingenuity of research and pains taking study may be better rewarded than that outlined in these few remarks upon tetany. It is a field wherein the interests of the pathologist, the clinician and the operating surgeon are common property, and he who properly harvests the seed already sown there may prove a benefactor to his race.

Etiologically the subject of tetany has nothing to do with that which must next engage our attention, namely tetanus. Yet, clinically they appear so closely related that those that ought to know better confuse them. Thus, I was informed, while abroad last summer, by a more than ordinarily intelligent physician that a well known European surgeon had lost so many patients from tetanus after removing the thyroid that he had been virtually forced to give up such operations. It required some pains to elicit the facts in the case, which simply were to the effect that he, like some others, had become discouraged on account of the proportion of cases which developed *tetany* after total extirpation of the thyroid. There would seem, then, to be no impropriety in proceeding at once to a consideration of some of the features of tetanus.

#### TETANUS.

Unlike tetany, tetanus is referred to in the oldest annals of medicine. One may find in Hypocrates, Galen and Celsus at least some indication of its principal symptoms, but its precise clinical history commenced with the end of the previous century, with the observations of Bajou and the grand work of Heurteloup which gives an excellent resume of the knowledge of his time. Fournier-Pescey extended this knowledge and showed the possibility of recovery. During the wars of the Empire clinical facts multiplied and we were given the accurate description of Larrey. It has remained for the second half of our own century to clearly discover the etiology and pathology of this disease.

Following the example of Richelot, in his Thesis of 1875, and of Mathieu, in his article in the Encyclopedic Dictionary, we must speak successively of the wounds, the wounded and the environment. First of all, any wound may present this complication, but some predispose more than others. The point of injury makes some difference. Wounds of the extremities, of the hands especially, seem more often to determine trismus than any others. Thus for Poland and for Yandell more than one half of the cases are due to traumas of the extremities. The character of the wound has been

alluded to by authors as occasioning a predisposition. Thus gun-shot wounds, especially the lacerated and contused, and next perhaps the injuries received from machinery, seem to be the most grave. The most cleanly cut wounds seem to be the least often infected, although tetanus in the past has, not rarely, followed amputations. On theoretic grounds, referring to the parasitic origin of the disease, it is not difficult to understand why it should more commonly follow ragged wounds. Burns, whether accidental or provoked by the actual cautery or by chemical substances, and frost-bites, whether superficial or deep, have also caused the disease, and as is well known, it frequently follows ligature of the umbilical cord in the new born. The extent and depth of the wound are features without importance. The prick of a needle, a hypodermic injection, the bite of a serpent, the penetration of a thorn, the extraction of a tooth, piercing the ears for ear rings, vaccination, dilatation of the nasal canal, the removal of an in-grown nail, and other equally trivial accidents or operations have been followed by the disease. In the past such operative measures as the constriction of a nerve in a stump, or the ligature *en masse* of the spermatic cord, or of the pedicle after ovariectomy, have been forbidden for this reason.

The presence in the wound of foreign bodies, of bullets or fragments of weapons, of thorns, of needles, and of any other small foreign particles, seems to predispose toward the disease. It has been generally supposed that an actual break of the surface by which air might be admitted, was a prerequisite for the manifestations of tetanus, but evidence is very strong that this is not absolutely necessary. The well known case of Morgagni in which it followed a contusion of the back, and such a case as that reported by Verneuil where it was apparently produced by a violent effort to prevent a fall, as well as cases reported by Bouchut, Macleod and others, put this all beyond a doubt. Closed fractures and small luxations or dislocations have likewise been followed by tetanus. A case has been reported by Richelot in which it followed the dislocation of a finger, and in which dissection revealed the nerves stretched over the dislocated extremity of the phalanx like violin strings. Such cases, therefore, are not so very rare.

Out of 121 cases observed by Wallace, in the Indies, 13 were of this character. Here also may be properly emphasized the fact that it may not occur until after cicatrization of a wound. Thus Cooper, Annandale, Larrey, Langenbeck and others have reported incontestable cases of this kind. I have myself seen, in consultation with Dr. Norton, then of Buffalo, a case of tetanus which resulted fatally, and which followed some weeks after complete healing of a tarsectomy wound, in an adult, made for the relief of club-foot. The patient had so completely recovered as to be up and about his work, when he was suddenly seized with the unmistakable symptoms of the disease.

The wounded individual is more or less predisposed according to circumstances of race, sex, age and constitution. The colored race are always more liable than the white. The negroes, Hindoos, Malayans and the islanders of Tonga and Fiji show a particularly unhappy disposition. That negroes are particularly liable was abundantly shown during our Civil War, and that the inhabitants of warm countries seem the less resistant is shown by the fact that in various European wars the Italians and the French have suffered more than the Russians and the Austrians. One ordinarily speaks of tetanus as a disease of adult life, yet infants are by no means exempt; and in the tropics the trismus of the new-born has caused a high rate of mortality. It was said by one plantation owner that fully three-fourths of the infants born upon his plantation succumbed to the disease. In Jamaica, according to Fournier-Pescey, a quarter of the new born Negroes succumb within eight days after their birth, and in Mexico and in Senegal the proportion is at times equally great. The ulceration around the ligature of the cord, or the little wound inflicted during the rite of circumcision, are the common causes of tetanus among these new-born, although it must be admitted that their detestable hygienic surroundings and their excessive poverty are contributing causes.

Men are attacked much more commonly than women, doubtless because their occupations expose them to more injuries, especially in war, males being commonly ten times as liable, according to some of our best authorities,—except

where climate, as above noted, especially predisposes. This difference is the more remarkable since parturition with its difficulties, and sometimes the necessary operative interferences, should make the disproportion less striking. In fact, much less serious injuries in the female have been followed by this disease. Thus, it has been known to follow amputation of the uterine neck, dilatation of the cervical canal by sponge tents, removal of polypus and ovariectomy.

Military surgeons have generally insisted that the mental and constitutional condition of patients figured largely in the etiology of the disease. Soldiers when worn out by fatigue or suffering from the disgrace of defeat or with their emotions vividly affected from any cause, are apparently more liable to the disease. The excitement of a sudden call to arms, of sudden discharge of cannon, even the whirring of bullets during the night, have been said to cause a shock which appeared to determine an invasion of the disease. Still, in 1870, says Mathieu, the besieged in Strasburg, Metz and Paris were affected with emotions even more vivid than those of the besiegers, and yet these last suffered more from tetanus; and thus after Waterloo the allied armies were less attacked than were the French, and so too in our Civil War not a single case was reported in the Confederate army, while the Federal troops lost 505 men from this source. Furthermore, those with visceral disease seem to be more subject to the disease. Malaria has also been supposed to be a contributing cause.

The influence of the environment is by no means the least interesting factor in the present consideration. The effect of climate is indisputable. Tetanus is *par excellence* a disease of hot countries. Guinea, Antilles, Senegal, Ceylon and Java have a reputation above all others. Military statistics show the same thing. In 1813 in Spain the English suffered in the proportion of one case of tetanus among eighty wounded men. In the East Indies in 1782 this proportion was doubled. In the war in Morocco there was one case of tetanus to nine hundred and twenty hospital patients of Spanish, and one to fifty-six of African birth. Apparently it is not heat alone which determines this intensity, so much as the combination of heat and humidity; still, quick variations of heat and cold,

such as warm days and cold nights, seem to exert a great effect. The sudden fall of temperature after the battles of Dresden and Bautzen, according to Larrey, caused a large number of cases. The electrical disturbances which accompany violent thunder storms seem to exert an influence, as do also cold winds saturated with moisture, like those which come from off the sea or sweep down the valleys of large rivers. Curiously enough the wounded who have been cared for in churches have suffered more from this disease than those cared for in any other way. After the battle of Jena, tetanus attacked especially the wounded who had been carried into churches. In 1870 after the battle of Sedan it was those who were thus cared for during the combat and the following night who were mostly attacked.

Verhoogen and Baert have recently published a memoir, dedicated to the Royal Society of Medical and Natural Sciences of Brussels, in which they cite at some length the endemic character of the disease in warmer climates, and in which they show the occasional epidemic character of the affection in man and even in some of the lower animals, and they cite as among the most startling evidences of this character the remarkable experience of Thiriart. He was unfortunate enough to lose by tetanus ten cases of major operations before he determined the source of the infection to exist in his hæmæstatic forceps. So soon as he thoroughly sterilized these by heat he had no further undesirable complications. If the disease can be so easily conveyed by instruments, the same is true of a midwife's scissors, and these latter may well be the cause of the terrible fatality of tetanus neonatorum of these same climates. These writers call attention also to the indefinite symptoms preceding the outbreak of the attack; the fever, the occurrence at times of epistaxis, the existence in many cases of a cutaneous rash resembling that of erysipelas, to the symptoms of kidney disease and the changes occurring in the kidneys, and to the enlargement of the spleen, as being all characteristic of the usual course of infectious disease.

The term *tetanus hydrophobicus* or *cephalic* tetanus has been applied to a somewhat peculiar manifestation of the disease first described by Bernard and Lepine.

When the injury by which the disease is provoked is located near the parts supplied by the cranial nerves the facial nerve has been supposed to be affected upon the same side; the lightest disturbance causes painful spasms of the neighboring muscles involved, and the pharynx and larynx, being virtually supplied by these nerves, when thus involved are so affected as to produce an intense dysphagia, with spasms of the glottis upon any effort to swallow even fluids; whence its misleading name of tetanus hydrophobicus. The poor patient suffering from these painful muscular spasms, which are provoked even by the sight of water or the thought of taking anything within the mouth, cyanosed, with spasmodic dyspnoea or temporary apnoea, presents a picture conforming well to the type imagined by the laity as that of a person in the last stage of hydrophobia.

Brunner has very recently experimentally studied this phase of the disease anew. He has determined that, in animals at least, the peculiar appearance of the face is due not to facial paralysis, but rather to a tonic tetanic spasm of muscles. This was made the more evident by a section of the facial nerve after appearance of this condition, whereupon it subsided at once. This is unquestionably the case also in patients thus affected, since it is impossible to understand how the parts supplied by the facial should be paralyzed while those supplied by the pneumogastric and hypoglossal should be thrown into violent spasm. (*Deut. Zeit. f. Chir.*, xxx.)

With regard to the etiology of tetanus, two theories have in the past had their strong advocates, or perhaps, to express it more accurately, the explanations that have been offered in the past can be best grouped under two distinct headings, as first the nervous theory, and second the humoral. The significance and intensity of the principal phenomena of tetanus have always pointed us so distinctly to the nervous system as the most active agent in the production of the disease, that it is not at all strange that the primary irritation has been located in some part of this system. Under this heading, however, must be ranged such explanations as that given by Forbes, who attributed the poisoning to a successive production of creatin and lactic acid, in consequence of exaggerated tissue degeneration; this latter he considered due to excessive nervous activity, and this last he left unexplained. Such an hypothesis as an ascending nervous irritation due to lesion of the peripheral nerve filaments, is, perhaps, the simplest that would offer, and has had numerous adherents in the past. Besides this, there have been many who regarded the disease as due to an excitation of the spinal cord, and by this have explained the increased temperature, the tendency to asphyxia, and some of the other phenomena peculiar to tetanus. According to Brown-Sequard, it is a pathological reflex, having

for its point of departure a peripheral nervous irritation, causing an undue functional activity in the superior portions of the medulla, which is followed by muscular contractions and elevation of temperature.

So far as the microscopic changes in tissues are concerned, there is much difference of opinion among authors. Rokitsansky and Demme have discovered changes in the neuroglia of the white matter in the spinal cord, which, however, Leyden does not consider to be pathological. Other authors like Clarke believe in congestion and softening of the grey matter, Dickinson in changes in both white and grey matter; while Lepelletier thought to have discovered a peripheral neuritis in these cases. The most exact observation of the nervous system of patients dying of tetanus, as well as of animals in whom the disease has been produced, do not reveal any changes, either in the central nervous system or in the peripheral. Nevertheless the whole course of the disease indicates a slow spread along the course of these nerves. The poison, whatever it is, probably reproducing itself in nerve substance spreads slowly toward the spinal cord, there to manifest its strongest activities. Elevation of temperature is by no means constant in experimental animals, it is seldom manifested. The exaggerated frequency of pulse is ascribed to a paralysis of the vagus.

On the other hand, the humoral theory has had its defenders, who have found plenty of facts upon which to base their views. According to these the alteration of the blood, which they have considered the exciting cause of tetanus, has been compared to poisons with various alkaloids, many of which are known to exert a selective influence on various organs or tissues. Defended especially in the past by Simpson and Travers, and more recently by Roser and Billroth, it supposes a specific toxæmia of the system, the unknown poison exerting a selective influence upon the nervous system. Others have regarded it as a toxæmia, due to poison generated directly in the wound, or to an autochthonous septicæmia, due to a sudden suppression of the functions of the skin, and the failure to eliminate its excretory products. The poison was supposed to be a chemical one, formed in the wound or near it, and thence absorbed into the blood. If this hypothesis were true we should have an evolution of the disease analogous to that of purulent inflammation. Quite recently, and in accordance with the tenets of the germ theory, the idea of a purely chemical poison has been abandoned, and the chief role assigned to micro-organisms. Before the parasitic nature

of the disease had been carefully recognized, Lister furnished a comparative proof of the truth of this hypothesis by showing how in six years under the antiseptic method, he had met with but two cases of tetanus, and these in wounds already septic.

Others yet have charged it with being distinctly a zymotic disease, which view had much in its favor, except the fact that until recently inoculation experiments had failed. Of course while each particular hypothesis under both the above headings had more or less in its favor there were objections which were fatal to each except to the last. For this last, namely that of zymosis, there were many corroborative facts, such as the statistics from the Dublin Lying-in Hospital, where there was at one time an epidemic of tetanus neonatorum; the mortality rate within the first fortnight being 17%, which was reduced to 5% after a better ventilation was established.

It has remained, however, for living observers, working within the past decade, to establish clearly the parasitic nature of this dread disease, and to isolate and investigate the organisms by which it is produced. In 1884 Carle and Rattone inoculated rabbits with an emulsion formed by macerating in distilled water a fragment of skin taken from a subject dying of lockjaw. Their results were positive. From them they concluded tetanus to be an infectious disease, but they could neither see nor cultivate the micro-organism which caused it.

The mere establishment of this fact was a very distinct advance in our knowledge of the natural history of the disease, and though some of their statements with regard to the biology of the micro-organisms which cause it, are hardly to be accepted, we, nevertheless, owe the above demonstration to them. During the year following Nicolaier demonstrated that in the ordinary soil of our gardens and streets there are bacteria which, when introduced under the integument of mice, guinea-pigs and rabbits, produce a typical tetanus with fatal termination. Inoculations made with dirt from the streets of Berlin, Leipsic and Wiesbaden gave the same results. Soon after this Rosenbach demonstrated to the German Congress of Surgeons (in 1886) that the same bacillus which Nicolaier described appeared in human tetanus, and soon after this his observations were confirmed by numerous observers.

## ROSWELL PARK.

In his communication to the Congress of Surgeons, Rosenbach first called attention to the fact that experiments had been made in a promising direction by Rose, Frickenhaus and by Arloing and Tripier, and that the latter had experimented in 1870 by injecting dogs and rabbits with blood and pus from tetanic patients, and had also vaccinated healthy horses with the blood of those suffering from this disease, but with negative result. He had himself injected into a dog 60° cc. of blood from a patient with tetanus, also without result; while Schültz and Billroth had done virtually the same thing, yet always with negative result. This was now explained by the fact that all these experimenters used dogs, which are known to be refractory to the disease. It was then that Carle and Rattone succeeded as mentioned above. They injected into 21 rabbits an emulsion made from the pus of an acne pustule, from which a fatal tetanus had developed, and they introduced it into the sciatic nerve sheath. Eleven of these animals died of tetanus. They recognized the fact that the pus so injected was swarming with micro-organisms, but had no success with cultivation experiment. It was in 1886 that Rosenbach made his first inoculation experiments by introducing a small piece of skin from the neighborhood of a wound of a patient dying of tetanus underneath the skin of guinea pigs and saw tetanus develop in each animal within a few hours. Similar experiments with skin from a part at some distance from the poisonous wound had no result. It was evident, therefore, that inoculation succeeded only with material taken directly from the infected spot. He succeeded also in transmitting the disease from animal to animal. These experiments agreed with those of Nicolaier, who got his material from black earth. Socin, Polaillon and Jeannel imitated him successfully, and Hochsinger and Bonome verified his experiments, as also did Shakespeare, of Philadelphia. Lumnitzer has multiplied these experiments and made a precise study of the bacillus of which we shall speak very shortly in some detail.

It will be seen from the above statement why writers in the past have with reason spoken of the telluric origin of tetanus. Quite recently in Paris Verneuil has strongly defended what may be called the equine origin of tetanus, according to which the earth which causes such lesions and which contains the tetanogenic germs is especially that which has received the dejections of the horse. Tetanus is known to occur very frequently among grooms and those who care for these animals, and falls from a horse and horse kicks are frequently alleged causes of the disease. (Horse dung seems especially suspicious material). It is least common of all among sailors, but when happening among them occurs almost exclusively on board ships used for the transportation of these animals. Numerous reported instances lend a certain degree of plausibility to these views, and they are entitled to at least respect, if not to complete credence. Within the past few weeks I have been called to attend a lad who was caring for a horse that

had developed a typical case of tetanus, but recovered therefrom. Before the horse was well the boy ran through the sole of his boot a rusty nail which projected from the floor of the shed in which this horse was kept. In just one week he developed the symptoms of tetanus and died within forty-eight hours. Of course it would be folly to think that the horse generated the germ or the poison, but the coincidence is certainly striking. All the specially infectious bacteria have their favorite soil; those of typhoid and cholera are found most often in water; those of suppuration about the skin and hair, and it is not difficult to admit at least that the germs of tetanus abound especially around the horse.

It is hardly necessary to detail the minutiae of Rosenbach's experiments. He found, as has every other observer, that the symptoms proceed in almost every instance from the point or part affected; that if it be in a limb that the poison was first introduced this limb is first involved in spasms, and that the so-called tetanus-hydrophobicus could be produced when the inoculation was made about the head or face. Examining the material with which he inoculated, he found a mixture of numerous forms, staphylococci, streptococci, diplococci, large and small bacilli, with and without spores. As one among these many forms he recognized the bacillus described by Nicolaie, but his best endeavors to make a pure culture of the specific organism failed. He even discovered that it or its spores were not destroyed by a temperature of 100° C. after five minutes exposure, and although by thus heating he killed off all or nearly all of the other organisms, he was still unable to make a pure culture of the one he was after.

It has remained for Kitasato to isolate, to cultivate and to study the organism in all its biological and pathological relations, and while he is not the discoverer of the organism, we owe to him mainly what we now know about it. He first worked with the pus from a patient dying three days after the onset of a typical tetanus, as well as with fragments of the splinter which caused the injury. In this material he found three forms of obligate anærobic bacteria, five facultative anærobic forms, and seven ærobic. The principal difficulty of course was to separate from these the particular organism which he wanted, and he succeeded by a method which those who desire to identify this organism will hereafter have to follow. He placed the mixture upon agar or blood serum, and then kept this in the thermostat at 38°C. for forty-eight hours, during which time the tetanus bacilli were stimulated into a

free formation of spores. The culture tubes were then placed in a water bath which was kept at 30°C. for from three-quarters of an hour to an hour. By this heat all the other organisms were destroyed and only the spores of the tetanus bacilli were left active. Inoculations of this into mice provoked the disease as typically as ever. He then planted these spores in gelatine and agar and cultivated them as anærobes in an atmosphere of hydrogen at a temperature of 18° to 20°C. And so by fresh refinements of technique which need hardly to be mentioned here he established that the tetanus bacilli might be cultivated in pure form, and that they grew as obligate anærobes with spore formation, their spores being extraordinarily resistant in the matter of temperature.

They are not necessarily killed by exposure to the air but grow only when the atmosphere is excluded. Under hydrogen they grow luxuriantly; under carbonic dioxide, not at all. The agar or gelatine in which they are planted must be very slightly but positively alkaline. They fluidify the gelatine with very slight formation of gas. If to the gelatine or agar 2% of sugar be added, their growth is more rapid, and it is even more so if to the culture material 0.1% sulphindigotate of sodium be added. They can even be grown in alkaline bouillon if hydrogen be present; they then generate a peculiar odor as if something were burnt. They can be cultivated from one generation to another without losing their virulence and without necessity for frequently passing them through animals. They may be grown on plates under hydrogen, but are ordinarily cultivated along the needle streak which very slowly, if at all, reaches the surface. They grow most rapidly at blood heat, very slowly at 20° C., but below 14° C. they do not grow at all. At blood temperature they form spores within 30 hours.

They have three principal phases of existence, *viz.*, a spore stage, a bacillus stage and a spore-bearing stage.

As grown in gelatine at ordinary temperature, they form separate bacilli, or gather in long threads. Where they form spores at higher temperature the spores are round and met with at one end of each bacillus, so as to give it a peculiar hat-pin or drum-stick shape. It stains best during this shape. They possess a very slight motility, which is better demonstrated on the warm stage. Bacilli which contain spores, apparently have no proper motion. They take the ordinary aniline colors well, and may be stained by Gram's method. The spore formation can be demonstrated to advantage by Ziehl's method of double staining. The bacillus seems to multiply by fission as well as by spores.

It is most interesting and important to know that the spore bacilli when dried by the ordinary method and then kept for

some days in an exsiccator over sulphuric acid, and then kept in ordinary atmosphere, preserve for months their virulence, and that their spores were found still acting by Kitasato after having been mixed with earth that had been sterilized in a steam apparatus for 10 hours. Evidently, then, tetanus spores are extremely resistant. Moist heat for an hour does not kill them, and, as Rosenbach had previously found, even five months' exposure to moist heat at 100 did not destroy them. Ten hours' exposure in 5 % carbolic acid left them still virulent; only after fifteen hours could they be thus destroyed. So also it took three hours' exposure in a 1 % sublimate solution, or thirty minutes in the same solution to which had been added 0.5 of 1 % of hydrochloric acid. To other chemicals they are equally resistant.

Kitasato left standing for two days a bouillon culture which he shook up with 10 cc. of chloroform. After the chloroform had been removed he injected several animals with the culture and found it pathogenic as ever, while fresh culture grew luxuriantly. When subcutaneously inoculated, small animals develop tetanic symptoms within twenty-four hours and die usually in less than seventy-two. Pigeons appear somewhat liable to the disease. It is evidently quite unnecessary that any foreign body should be introduced along with the active germs, as would perhaps appear from a study of the well-known features of the disease. Ordinarily there is no local reaction at all, and on a section when a splinter has been used, one finds it embedded in a mass of leucocytes without other disturbance.

It is to be emphasized that the symptoms of tetanus are almost invariably at first local, the muscles being first involved at that part where the inoculation was practiced. It is furthermore noteworthy that by the microscope these organisms are never found at any distance from the wound, and that, moreover, even here they perish within less than twenty-four hours, except as they may be found in the pus. Most careful examinations of the brain, the nerves, the muscles, the viscera and even the blood fail to reveal the slightest trace of them, and inoculations practiced with these tissues or fluids are almost always without results.

It is also of great interest that only tissues from the immediate neighborhood of such a splinter are infectious, and that inoculations with blood, brain, nerves or other organs of the animal have never caused the disease. Possibly in the above

fact we may find an explanation of some of the cases above referred to, those of the disease supervening long after the healing of a wound, since the period of incubation in man is known to vary within wide limits.

Such a case has indeed been reported by Renvers from Leyden's Clinic. Deep in the sole of the foot was found a splinter of wood an inch long. Inoculations with particles from this splinter succeeded, while those made with tissue only 3 millimetres distant from it produced no disease.

Kitasato trephined animals and then inoculated the dura with a pure culture, but after their death was unable to find the slightest trace of the bacilli in the brain tissues or in the blood; while culture experiments with the same all failed. These statements are somewhat at variance with those made by some earlier experimenters, yet they appear to bear the stamp of certainty, and have been corroborated by many other investigators. In order to demonstrate their action still further Kitasato practiced inoculations as before, which were followed within half an hour to four hours by excision of the inoculated area and cauterization of the wound thus made with the actual cautery. The animals died just as if nothing had interfered with the virulence of the disease.

Repeating these experiments several times, I have myself obtained the same results. Although it has seemed to me as if the onset of the symptoms were somewhat postponed and the progress of the disease somewhat delayed. The rapidity with which all bacilli vanish from all the tissues and juices of the body is perhaps the most astonishing feature of the disease. Presumably they generate a poison whose effects are far-reaching, and this poison has been studied by Kitasato and Weyl, who have very recently published a further communication upon the subject. The conclusions arrived at by Kitasato are briefly as follows:

1. Tetanus is a specific disease.
2. The active agent in producing it is a bacillus which is identical with that described by Nicolaier and later studied by Rosenbach, and now determined to be an anærobic organism.
3. This bacillus is found in the pus from tetanic patients and

animals. It often forms spores in such pus, nevertheless may be frequently met with while free from spores.

4. It is possible to cultivate this bacillus from such pus, and with pure cultures of it to reproduce tetanus in animals.

5. The somewhat contradictory statements of early observers find their explanation in the fact that tetanus is met with in various stages, and that the more quickly the animals die from the disease, the more likely are we to find spores in the bacilli. But these bacilli are, or have been, always present, and from them one can always cultivate spore-bearing descendants.

A consideration of the specific factors involved in tetanus, is inseparable from that of the toxins or ptomaines which they produce. During the period intervening between the time of inoculation, and the first symptoms of the disease, there probably occurs a gradual increase in the numbers of the micro-organisms, while there is slowly elaborated an increasing amount of those toxic substances. These are at first eliminated probably by the skin and kidneys as rapidly as formed, but they finally accumulate sufficiently to display their activities, first upon the nervous system, and later by the usual symptoms and signs of the disease as well known. It is corroborative of such view that the administration of full doses of pilocarpine in the early treatment of the disease is followed by benefit. The common treatment of the disease as well denotes the same, since the chloral so often given tends to lessen the recognition of afferent impulses, and the bromides to decrease the force of the motor explosion following. (*Med. News.*)

Since Kitasato published his first formal paper in the *Zeitschrift f. Hygiene*, he and Weyl have made three communications upon the ptomaines or poisons by which the bacilli produce the symptoms of tetanus. As is well known Brieger isolated from cultures of tetanus bacilli a crystalline material which he named tetanin. Working with the hydrochlorate of this alkaloid the above observers demonstrated that it produces in mice spasmodic disturbances, and increased flow of saliva.

Another analogous substance separated from cultures in the same way has been called by Brieger, tetanotoxin. Their experiments with this material produced results which were also analogous, and yet it appears from their work that the dose of either of these alkaloids must be relatively so great that one is forced to the conclusion that the tetanus bacillus in the living organism produces a poison of much greater virulence than

either of these yet isolated. They promise further studies and the publication of their results.

The investigations of Dr. Shakespeare, of Philadelphia, also deserve mention here. He was able by placing in contact with the central nervous system of healthy rabbits infusions of the spinal cords of tetanic cases, to speedily produce characteristic symptoms of the disease, while the subcutaneous injection of the same material had no effect. Although during his experiments he failed to discover specific micro-organisms, he nevertheless showed what has been demonstrated in another way by others, that the exclusion of the tetanogenic spores by extirpation of the infected sore, or by amputation of the limb in which it occurs, with distinct failure to arrest the disease, confirm the idea of local activity, combined with the elaboration of poisonous matters circulating in the blood. (*Med. News*, Oct. 25, 1890.)

Among very recent experiments concerning tetanus are those of Babes and Puscariu. (*Centrablt. f. Bakteriologie*, VIII. No. 3.)

They worked with cultures received from Kitasato as well as with those which they isolated from horses suffering from the disease. From those animals which died as a result of inoculations, only the bacillus from the point of inoculation could be cultivated, but nothing from the veins, or internal organs, nor from the brain or spinal cord. Nevertheless, mice and rabbits which received small doses of these fluids died from some poisoning without tetanic symptoms.

For purposes of experiment, two mice and two rabbits were inoculated with emulsion of brain tissue from a rabbit dying with tetanus. The former died in four days, the latter in eight, without symptoms of tetanus. In the endeavor to discover or invent a protective injection, these experiments were repeated and the emulsions were made with bouillon in different strengths, but the animals nearly all died.

Babes prepared an albumose out of agar cultures which did not contain peptone, whose watery solution was passed several times through a Chamberland filter. This substance sometimes, but not always, produced tetanic symptoms with cramps and paralysis, and fatal results after varying lengths of time.

Tizzoni, Cattani and Baquis have investigated three cases of tetanus, from which they isolated five different forms of bacteria, of which two only were pathogenic. The first of these seems to be identical with that described by Kitasato. The second was recovered from the blood and spleen of an animal dying after subcutaneous injection of specific pus.

It was also a bacillus smaller than the other, having involution forms and producing spores. It also showed itself to be anaerobic. After subcutaneous injection, typical tetanus was produced in most of the smaller animals. These authors were not able to deny, however, that this organism might not be identical with Kitasato's.

They claim that both of these bacilli lose somewhat of their virulent power with time and peculiarity of culture medium. They, like Kitasato, found no protection from excising the point of inoculation. (*Zeigler's Beiträge*, vii, 4.)

A recognition of the minute causes of tetanus raises the question as to what can be done for the disease. Evidently the bacilli themselves remain at the point where first introduced, while the poison which they produce circulates. Numerous observations seem to prove that this poison can be antidoted by reasonably strong solutions of various antiseptics; 5% carbolic solution, or 1% of nitrate of silver, or bichloride of mercury destroy the germs in the culture tubes; so also does exposure to steam for five minutes. The German writers seem to have confidence in iodoform when packed into the wound. The anærobic organisms, to which these bacilli belong, have a powerful reducing action, and are therefore capable of splitting up iodoform and of producing iodine in pure or nascent condition. In experiments upon animals, 10% solutions of iodoform in ether applied to the point of inoculation within an hour afterward have sufficed to prevent the development of the disease, but all experiments go to prove that whatever is done must be done within a very short time after the inoculation. The uselessness of amputation in well marked cases is very plain from the above experiments, as well as of any other destructive or mutilating operation. The method by incision recommended by Bilguer, by which air was freely admitted to the tissues, has in it something to recommend itself. Of course the very earliest possible removal of the foreign body should be effected. Military experiences show that recovery has sometimes followed the removal of the irritating substance. Isolation, nutrition and stimulation, with such drugs as may control symptoms, sum up the internal treatment of these cases.

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